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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,947	12/08/2003	Bettina Mockel	021123-0306724	9845

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PILLSBURY WINTHROP LLP
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EXAMINER

RAGHU, GANAPATHIRAM

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/728,947

Applicant(s)

MOCKEL ET AL.

Examiner

Ganapathirama Raghu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 10/728947.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>Dec 8, 2003</u> | 6) <input checked="" type="checkbox"/> Other: <u>Sequence alignments</u> |

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DETAILED ACTION

New claims 24-34 are pending in this application for examination.

Priority

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/860768, filed on 05/21/2001.

Specification

The disclosure is objected to because of the following informalities:

Examiner notes that applicants have not updated the relationship of the instant application to its parent application that has matured in to a US patent. Examiner urges applicants to amend said information by providing the US patent number in response to this office action.

In addition, please note the following:

1. Page 11, Line-26 and Page 13, Line-29: Binomial Nomenclature convention; "Corynebacterium glutamicum".

Appropriate correction is required.

Claim Rejections

35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claim 34 is rejected under 35 U.S.C. 101 because the claim could read on a non-statutory subject matter. The claim is drawn to a 'host cell', which could still be attached to the host such as human. Claims directed to such matter are considered non-statutory. Examiner suggests amending the claim to recite 'an isolated host cell' in order to overcome the rejection.

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24 and 31 and claims 25-26, 32, 34 that depend therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24 recites the phrase "as set forth in SEQ ID NO: 1". It is not clear to the examiner whether as to what this phrase means in the context of the above claim. It is not clear whether the isolated nucleic acid indeed actually has the sequence SEQ ID NO: 1 or whether SEQ ID NO: 1 is a representative sequence of the isolated polynucleotide. Examiner suggests applicants to make a direct reference to the SEQ ID NO: 1 such as "a polynucleotide sequence SEQ ID NO: 1".

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "functionally neutral sense mutation" in claim 26 does

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not clearly state whether the sense mutations are referring to the codons in the polynucleotide sequence or to the enzyme activity whose function is not affected by the changes in the polynucleotide and the corresponding change in the polypeptide.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 31 recites the phrase "as set forth in SEQ ID NO: 3". It is not clear to the examiner whether as to what this phrase means in the context of the above claim. It is not clear whether the isolated nucleic acid indeed actually has the sequence SEQ ID NO: 3 or whether SEQ ID NO: 3 is a representative sequence of the isolated polynucleotide. Examiner suggests applicants to make a direct reference to the SEQ ID NO: 3 such as "a polynucleotide sequence SEQ ID NO: 3".

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 29 recites the phrase "amino acid sequence as set out in SEQ ID NO: 3". It is not clear to the examiner whether as to what this phrase means in the context of the above claim. It is not clear whether the isolated amino acid indeed actually has the sequence SEQ ID NO: 3 or whether SEQ ID NO: 3 is a representative sequence of the isolated polypeptide. Examiner suggests applicants to make a direct reference to the SEQ ID NO: 3 such as "a polypeptide sequence SEQ ID NO: 3".

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Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 33 is drawn to 'the vector of claim 35', a non-existing claim as the metes and bounds are not clear. If the claim is drawn to claim 32, the rejection still holds, as claims 32 and 33 are dependent on a rejected claim 31.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide with SEQ ID NO: 1 encoding a polypeptide with SEQ ID NO: 2 having a enolase activity, does not reasonably provide enablement for any polynucleotide encoding a polypeptide having 90% and 95% amino acid sequence identity to SEQ ID NO: 2 and wherein the said polypeptide has enolase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the

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nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 29 and 30 are so broad as to encompass any polynucleotide encoding a polypeptide having enolase activity and an amino acid sequence that is 90% to 95% sequence identity to SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one enolase. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides. The specification is limited to teaching the use of SEQ ID NO: 1 as the polynucleotide which encodes SEQ ID NO: 2 as an enolase, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp.

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433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide encoding a polypeptide with 90 to 95% identity to the SEQ ID NO: 2 because the specification does not establish: (A) regions of the protein/polynucleotide structure which may be modified without affecting the encoded enolase activity; (B) the general tolerance of polynucleotide encoding enolase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

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with the scope of the claims broadly including polynucleotides with an enormous number of modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 27, 29-30, 32-34 are rejected under 35 U.S.C. 102 (e) as being anticipated by Pompejus et al., Claim 27 is drawn to a fragment of SEQ ID NO: 1 encoding a polypeptide that has enolase activity. Claims 29-30 are drawn to an isolated polynucleotide encoding a polypeptide that has an amino acid sequence that is at least 90% or 95% identity to SEQ ID NO: 2. Claims 32 and 34 are drawn to vectors and host cell comprising the polynucleotide of claim 27. Pompejus et al., (US 2004/0180408 A1. Pub Date 9/16/2004), disclose an isolated

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polynucleotide sequence (SEQ ID NO: 71) which is 88.5% homology to the SEQ ID NO: 1, i.e., fragment of SEQ ID NO: 1, that encodes a polypeptide having enolase activity. Furthermore said polynucleotide of Pompejus et al., encodes a polypeptide that has an amino acid sequence that is 99.7% identical to SEQ ID NO: 2. The reference also discloses vectors and host cells comprising said polynucleotides. Therefore, Pompejus et al., anticipate claims 27, 29, 30, 32 and 34 as written (see copy of the sequence alignments provided).

Conclusion

None of the claims are allowed.

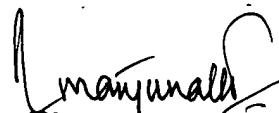
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached on 8 am - 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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September 25, 2005



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PRIMARY EXAMINER